

# PATENT SPECIFICATION

(11) 1 226 448

NO DRAWINGS

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- (21) Application No. 35099/69 (22) Filed 11 July 1969  
 (31) Convention Application No. 153 128 (32) Filed 15 July 1968 in  
 (33) New Zealand (NZ)  
 (45) Complete Specification published 31 March 1971  
 (51) International Classification C 08 b 15/00  
 (52) Index at acceptance  
 C3A 2



NATIONAL REFERENCE  
 LIBRARY OF SCIENCE  
 AND INVENTION

## (54) IMPROVEMENTS IN OR RELATING TO ION EXCHANGE MATERIALS

(71) We, TASMAN VACCINE LABORATORY LIMITED of 35 Whakatiki Street, Upper Hutt, New Zealand, a Company organised according to the laws of New Zealand, do hereby declare the invention for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be described in and by the following statement:—

10 This invention relates to ion exchange materials. In general an ion exchange resin consists of an inert insoluble substrate or matrix into which are introduced ionizable chemical groups. Such active chemical groups may be either basic or acidic in nature and capable of binding anions or cations respectively by a process analogous to salt formation. Such bound ions may be exchanged for different ions when the chemical environment of the resin is changed, e.g. in the process of water softening sodium ions are exchanged for calcium and magnesium ions.

25 Chemical substrates useful for preparing ion exchange materials can be prepared from the condensation of phenols with formaldehyde or the polymerisation of monomers such as styrene, divinylbenzene or methacrylic acid. One requisite of such a substrate

fibrous cellulose have very restricted application whereas the synthetic ion exchange resins are usually produced in granular or bead form having good hydraulic properties and hence very broad fields of application, but as stated the introduction of active chemical groups is not always easy to carry out.

On the other hand, although it has also been proposed to use certain types of regenerated cellulose as ion-exchange materials, and regenerated cellulose is obtainable in granular form, it is found that, if the number of ionisable groups attached to the cellulose exceeds a certain level, then the resultant material becomes soluble in dilute acid and alkali. As ion-exchange purification often involves regeneration with acidic or alkaline media this is highly inconvenient.

According to this invention we provide a method of making an ion-exchanger comprising the introduction of cross-linking residues into regenerated cellulose together with or followed by the introduction of exchange groups capable of anion or cation exchange into the cellulose, the cross-linking being carried out in the reaction medium free from components capable of reacting readily with the cross-linking residues under

but this requisite is not always met by such substrates as have been prepared in the past.

35 Cellulose is a naturally occurring substrate which is insoluble in water and which can be easily chemically modified to incorporate ionizable groups. However, cellulose has a fibrous structure and hence ion exchange materials based on cellulose usually suffer from the disadvantage of poor hydraulic properties and generally have low flow rates and tend to become easily clogged by particles of suspended matter. Consequently ion exchange materials based on

[Price 25p]

The regenerated cellulose may be, for example, obtained from viscose and may be in a variety of forms such as rod, filament, yarn, woven cloth, flakes, beads, granules, powder, sponge, tube or sheet. The cellulose may contain softeners or plasticisers such as glycerol, urea or triethylene glycol and may contain a preservative such as phenol.

The cross-linking of the regenerated cellulose may be carried out chemically, by the use of any bifunctional chemical compound capable of reacting with two hydroxyl

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groups to form covalent bonds such as by the treatment of regenerated cellulose with an aldehyde under acidic conditions, to give an ion exchanger cross-linked by aldehyde residues, e.g. formaldehyde residues. Suitable aldehydes are formaldehyde, glyoxal, glutaraldehyde and acrolein and the acid may conveniently be hydrochloric acid. Alternatively, the cross-linking may be achieved by treatment of the cellulose with epichlorhydrin under basic conditions preferably using sodium hydroxide. Alternatively, cross-linking may be achieved physically by exposure of the regenerated cellulose to high intensity ionising radiation such as that afforded by ultra-violet light, gamma rays or electron beams, in the presence of water and sensitizing chemicals.

The properties of the cross-linked regenerated cellulose may be further modified by the introduction of non-ionising chemical groups such as methyl, ethyl, phenyl or cyclohexyl groups, for example in order to enhance the hydrophobic properties of the final product.

Preferably, the degree of cross-linking required to confer the necessary properties to the regenerated cellulose may vary from 1 to 10 per cent, although occasionally degrees of cross-linking outside this range may be required for special reasons. The degree of cross-linking is expressed in terms of the ratio of the weight of cross-linking agent to the dry weight of the regenerated cellulose.

A great variety of exchange groups may be introduced to the regenerated cellulose, either after the cross-linking or at the same time as the cross-linking reaction. As explained above, it is essential that the cross-linking be carried out in a reaction medium free of components capable of reacting readily with the cross-linking residues under the conditions employed to give terminal

groups. The introduction of exchange groups may be carried out simultaneously with the cross-linking reaction. Groups capable of cross-linking reaction. Groups capable of anion exchange which may be introduced include amino, alkylamino, guanidino, and quaternary ammonium groups. Groups capable of cation exchange which may be introduced include sulphonic acids, phosphate and carboxyl groups.

It has been found that for both the cross-linking reaction and the introduction of the exchanger groups the water content of the reaction mixture should be carefully controlled. In general, the water content lies within the range of 50 to 100 per cent of the weight of the regenerated cellulose and depends somewhat on the grain size of the cellulose used.

The invention will now be further illustrated with reference to the following Examples. Examples 1 to 5 illustrate various methods of preparation of ion exchangers in accordance with the invention. Example 6 illustrates the advantage of an ion exchanger obtained in accordance with the invention when compared with a regenerated cellulose which has not been cross-linked. Examples 7 and 8 illustrate the use of the ion exchange materials prepared in accordance with the invention in the separation of protein-containing materials. Mesh sizes are in accordance with British Standard 410/62, published in 1963.

#### EXAMPLE 1

Ground dried regenerated cellulose tubing (obtained from viscose) (obtained from the Viscose Development Company Limited, South Dock, Swansea) was subjected to further grinding in a Christy and Norris laboratory mill to produce a fraction in the size range 30-50 mesh by sieving. 200 grams of this fraction were placed in 1 litre of 10 per cent (W/V) formaldehyde containing 2 per cent (W/V) hydrochloric acid for 48 hours at room temperature. The cross-linked regenerated cellulose so obtained was separated from the solution and thoroughly washed with cold tap water, and finally dried in a hot air oven at 100°C.

The dry cross-linked regenerated cellulose was then mixed with monochloroacetic acid (30 grams) in 30 per cent (W/V) sodium hydroxide (145 ml). After thorough incorporation of the reagents into the regenerated cellulose, the mixture, which appeared fairly dry at this stage, was placed in a screw cap jar and lightly pressed down. The lid was placed on the jar and the jar allowed to stand for 30 minutes and then placed in a water bath so that the water, covered the jar up to the level of the mixture. The water was brought to the boil and allowed to boil for exactly 1 hour. The jar was removed, cooled and the contents (now

of cold water) stirred. The resultant ion exchange material was filtered on a large Buchner funnel and washed with deionised water until the washings were neutral. The ion exchange material was dried and the final product (H form) had an exchange capacity of approximately 0.9 milliequivalents per gram.

#### EXAMPLE 2

Monofilament regenerated cellulose obtained from viscose, (25,000 denier gauge, obtained from Lustre Fibres Limited, of Coventry) was finely ground in a Christy and Norris laboratory mill to produce a fraction of 100-150 standard mesh size. 200 grams of this fraction were thoroughly mixed with 30 per cent sodium hydroxide

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solution (200 ml) to which diethylaminoethyl chloride hydrochloride (66 grams) and epichlorhydrin (5 ml) had been added. The mixing was done under a hood filter with an extractor fan. The mixture, which appeared dry, was placed in a screw topped jar and lightly compressed, the lid placed on the jar and the jar allowed to stand for 30 minutes. The jar was placed in a boiling water bath for 1 hour and then allowed to cool. The contents were tipped into 5 litres of cold water, stirred, allowed to settle and the brown supernatant removed by decantation. The process was repeated till the supernatant was approximately neutral. The ion exchange material was collected by filtration and air dried. The dry material had an exchange capacity calculated from uptake of hydrochloric acid of 0.9 milliequivalents per gram.

#### EXAMPLE 3

Ground dried regenerated cellulose tubing obtained from viscose (18 to 30 mesh size, obtained from The Viscose Development Company Limited, South Dock Swansea) (200 grams) was mixed with 30 per cent (W/V) sodium hydroxide (144 ml) which had been previously mixed with monochloroacetic acid (30 grams) and epichlorhydrin (5 ml). The final mixture, which appeared almost dry, was placed in a screw cap jar and lightly compressed, after which the lid was placed on the jar and the jar allowed to stand for 30 minutes before being placed in boiling water bath for 1 hour. After cooling, the contents were tipped into 5 litres of cold 1-N sulphuric acid. The resultant ion exchange material was washed several times by decantation and resuspension in water until the supernatant solution was neutral. The product was then collected by filtration and air dried. The dry material had an exchange capacity calculated from titration with 0.1N

meter of 0.8 milliequivalents per gram.

#### EXAMPLE 4

Ground regenerated cellulose monofilament obtained from viscose (obtained from Lustre Fibres Limited (Coventry) and of 18-30 mesh range (240 grams) was placed in 1 litre of 10 per cent (W/V) formaldehyde solution containing 2 per cent (W/V) hydrochloric acid. The mixture was allowed to stand at room temperature for 48 hours, after which the cross-linked regenerated cellulose was collected by filtration, washed with water and dried in a hot air oven at 100°C.

The dry cross-linked regenerated cellulose was then mixed with 30 per cent (W/V) sodium hydroxide solution (145 ml) previously mixed with diethylaminoethyl

chloride hydrochloride (80 grams). The mixture was placed in a screw top jar and allowed to stand for 30 minutes before being heated for 1 hour in a boiling water bath. After cooling, the contents were tipped with vigorous stirring into 5 litres of cold water. After settling, the brown supernatant liquid was removed by decantation and the product washed by resuspension in water and decantation until the supernatant liquid was colourless and neutral. The product was collected by filtration and air dried. The dry product had an exchange capacity calculated from the uptake of hydrochloric acid of 0.9 milliequivalents per gram.

#### EXAMPLE 5

Regenerated cellulose obtained from viscose (100 grams) of 30-50 mesh was sprayed with epichlorhydrin (10 ml) so that it was evenly coated. 30 per cent (W/V) sodium hydroxide (75 ml) was added and thoroughly mixed in. After standing for 30 minutes, the mixture was heated for 1 hour at 100°C in a stoppered container. The cross-linked regenerated cellulose obtained was washed with water and dried.

The product (25 grams) was mixed with 85 per cent orthophosphoric acid (11 ml) and urea (32 grams) dissolved in water (32 ml). The mixture was heated at 140°C for 5 hours. The dry product after isolation had an exchange capacity (based on the splitting of 5 per cent sodium chloride solution) of 2.7 milliequivalents per gram.

#### EXAMPLE 6

Regenerated cellulose obtained from viscose (20 grams) of 30-50 mesh size was converted into anion exchange material by treatment with diethylaminoethyl chloride hydrochloride (6 grams) and 30 per cent sodium hydroxide (12 ml) and heated for 1 hour at 100°C as described in Example 2.

The treatment was repeated with a further regenerated cellulose except that

mixture before heating.

The initial uncross-linked ion exchange material swelled and dissolved in 10 per cent sodium hydroxide solution. The cross-linked exchange material had not dissolved in the alkali after 1 week and the grains only showed slight swelling.

#### EXAMPLE 7

An ion exchange material obtained from the treatment of regenerated cellulose according to Example 2 was made into a slurry with water and poured into a glass tube of 2 cm. in diameter to give a 25 cm. high resin column. The column was equilibrated with phosphate buffer solution pH 8 by first passing through 250 ml of the buffer at 0.5 M concentration followed by

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250 mls of 0.005M buffer. The excess buffer was removed from the top of the column and goat serum (0.5 ml) applied and allowed to soak in. The column was then eluted using a buffer gradient at a pumping rate of 2 mls per minute with buffer concentration increasing from 0.005M to 0.25M. The output from the bottom of the column was monitored with an ultra violet spectrophotometer at 280 m $\mu$ . The graph showed the separation of the serum into 5 well defined peaks corresponding to serum albumin, and  $\alpha_1$ ,  $\alpha_2$ ,  $\beta$  and  $\gamma$  globulin.

#### 15 EXAMPLE 8

A column of the carboxymethyl derivative of cross-linked regenerated cellulose, obtained from viscose was used to selectively absorb lysozyme from a mixture of egg white proteins. The column was operated in the sodium form and lysozyme was recovered by elution with 10 per cent brine.

The above experiments show the preparation and the use of ion exchange materials with hydraulic properties which enable high flow rates to be obtained with viscous liquids, such as sugar syrups containing high percentage of solids. The hydraulic properties can be varied over a wide range simply by altering the mesh size range of the grains, thus contrasting with the limited applicability of ordinary fibrous cellulose. The resin granules have good physical stability and do not tend to gelatinize in alkali, as is the case with normal cellulose exchangers. The degree of swelling of the resin grains can be readily controlled by varying the degree of cross-linking. The physical nature of the ion exchange resins prepared in accordance with the invention enables them to be used for liquids containing large amounts of suspended particulate matter, such as would be the case for example in purifying effluent from a meat works, which would

changer and ion exchange cellulose ex-  
acceptable level for commercial application. Furthermore, with the granular exchangers of the present invention, it is a straightforward operation to backwash the column and free the resin from trapped particulate matter so that the resin can be reused.

#### WHAT WE CLAIM IS:—

1. A method of making an ion exchanger comprising the introduction of cross-linking residues into regenerated cellulose together with or followed by the introduction of exchange groups capable of anion or cation exchange into the cellulose, the cross-linking being carried out in a reaction medium free of components capable of reacting readily with the cross-linking residues under the conditions employed to give terminal groups.

2. A method of making an ion exchanger according to claim 1 wherein the regenerated cellulose is obtained from viscose.

3. A method of making an ion exchanger according to claim 1 or 2 wherein the introduced exchange groups are capable of anion exchange and chosen from amino, alkylamino, guanidino, and quaternary ammonium groups.

4. A method of making an ion exchanger according to claim 1 or 2 wherein the introduced exchange groups are capable of cation exchange and chosen from sulfonic acid, phosphate and carboxyl groups.

5. A method of making an ion exchanger according to any one of claims 1 to 4 wherein the cross-linking residues are introduced by treatment of the regenerated cellulose with an aldehyde under acidic conditions.

6. A method of making an ion exchanger according to claim 5 wherein the aldehyde is formaldehyde and the reaction is conducted in the presence of hydrochloric acid.

7. A method of making an ion exchanger according to any one of claims 1 to 4 wherein the cross-linking residues are introduced by treatment of the cellulose with epichlorhydrin under basic conditions.

8. A method of making an ion exchanger according to claim 7 wherein the base used is sodium hydroxide.

9. A method of making an ion exchanger according to any one of the preceding claims wherein the degree of cross-linking is from 1 to 10 per cent, based on the ratio of weight of cross-linking agent to the dry weight of the regenerated cellulose.

10. A method of making an ion exchanger according to any one of the preceding claims wherein the water content during the cross-linking and the introduction of the exchange groups lies within the range of 50 to 100 per cent of the weight of regenerated cellulose.

11. An ion exchanger prepared by the

12. An ion exchanger prepared by aldehyde regenerated cellulose cross-linked by aldehyde residues and having exchange groups capable of anion or cation exchange attached to the cellulose.

13. An ion exchanger according to claim 12 wherein the aldehyde residues are formaldehyde residues.

14. An ion exchanger according to claim 12 or 13 wherein the regenerated cellulose is obtained from viscose.

15. An ion exchanger according to any one of claims 11 to 14 wherein the exchange groups are capable of anion exchange and chosen from amino, alkylamino, guanidino or quaternary ammonium.

16. An ion exchanger according to any one of claims 11 to 14 wherein the exchange

groups are capable of cation exchange and chosen from sulfonic acid, phosphate or carboxyl groups.

17. A method of making an ion exchanger according to claim 1 substantially as described herein with reference to any one of Examples 1 to 5.

18. An ion exchanger according to claim 12 substantially as described herein with reference to any one of Examples 1 to 5.

MEWBURN ELLIS & CO.,

Chartered Patent Agents,

70-72 Chancery Lane,  
London, W.C.2.

Agents for the Applicants.

Printed for Her Majesty's Stationery Office by The Tweeddale Press Ltd., Berwick-upon-Tweed, 1971  
Published at the Patent Office, 25 Southampton Buildings, London WC2A 1AY from which copies may be obtained.

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